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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,537	09/13/2001	Gene M. Shearer	4239-60808	7176

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EXAMINER

BELYAVSKYI, MICHAEL A

ART UNIT PAPER NUMBER

1644

DATE MAILED: 03/25/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/936,537

Applicant(s)

SHEARER ET AL.

Examiner

Michael A Belyavskiy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 08 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 18-24, 26, 27 and 29-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-17, 25 and 28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 13 September 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 1-33 are pending.

1. Applicant's election with traverse of Group I, claims 1-17, 25 and 28 and multiple sclerosis as species of autoimmune disease, myelin basic protein as species of autoantigenic protein, monocytes as species of APC and SNB19 as species of glioblastoma cell in Paper No. 7 is acknowledged. The traversal is on the grounds that: (i) the unity of invention was found during the international proceeding only for claims 18-19 and 26-27 and (ii) there would be no undue search burden on the examiner. This is not found persuasive because CFR 1.475 (a) indicates that a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. CFR 1.475(e) indicates that the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim (MPEP R-90 -- R-91 and 1893.03(d)).

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical feature of Group I is considered to be a method of specifically inhibiting an immune response by inducing apoptosis. The special technical feature of Group II is considered to be a method of specifically inhibiting an immune response by inducing anergy. The special technical feature of Group III is considered to be a method of specifically inhibiting an immune response by inducing apoptosis and anergy. The special technical feature of Group IV is considered to be an immunosuppressive composition comprising one or more factors secreted by glioblastoma cells. The special technical feature of Group V is considered to be a method for enhancing tolerance in a host to an allogenic donor graft. The special technical feature of Group VI is considered to be a method for enhancing tolerance in a host to an autoantigen. The special technical feature of Group VII is considered to be a method of making an immunosuppressive composition comprising APC. The special technical feature of Group VIII is considered to be an immunosuppressive composition, comprising APC.

Accordingly, Groups I-VIII are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

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The requirement is still deemed proper and is therefore made FINAL.

Claims 18-24, 26-27 and 29-33 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-17, 25 and 28 are under consideration in the instant application.

2. Applicant's IDS, filed 09/13/01 is acknowledged, however, the citations lacking the date and page numbers have been crossed out. Applicant is required to provide the date and page numbers for said citation. In addition, all ATCC citation have been crossed out because more complete information, such as the date of the publication and catalog number are required.

3. It is noted that Brief Description of the Figures recites 11 figures, however there are 13 submitted figures.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-17, 25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Base claim 1 and dependent claims 2-17 and 25 are rejected under 35 U.S.C. 112, second paragraph, because claim 1 being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted step are: The omitted step is resolution step: it is unclear how specifically inhibiting an immune response by just *ex-vivo* exposing purified APC to an immunosuppressive composition, as recited in claim 1.

B. Claim 17 is indefinite in the recitation of "SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell" because its characteristics are not known. The use of "SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG " as the sole means of identifying the claimed cell lines render the claim indefinite because " SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG " are merely laboratory designations which do not clearly define the claimed products, since different laboratories may use the same laboratory designations to define completely cell lines .

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Amending the claim to recite the appropriate ATCC Accession Number would obviate this rejection.

C. Claim 28 is indefinite and ambiguous in being dependent upon non-elected claim 18.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines are required to practice the claimed invention. As a required elements, they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit said cell lines. See 37 CFR 1.801-1.809.

If the deposit have been made under the terms of the Budapest treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the cell lines has been deposited under the Budapest Treaty and that the cell lines will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or for the enforceable life of the patent whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the Budapest treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in position to make such assurances, or statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met

It is noted that Applicant indicated that said cell lines are available from ATCC (IDS).

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However, applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from ATCC, nor is there sufficient evidence as to the ATCC policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. There is no objective evidence that the SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines will be readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

7. Claims 1-17, 25 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of specifically inhibiting an immune response to one or more selected antigen, comprising exposing purified or isolated APC to a specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17, that secreted by SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines, does not reasonably provide enablement for a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to *any* factor secreted by *any* glioblastoma cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

The specification disclosed only a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to a specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17, that secreted by SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines. The instant claims encompass in their breadth: a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to *any* factors secreted by *any* glioblastoma cell.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

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Applicant has not provided sufficient biochemical information that distinctly identifies such "immunosuppressive factors" that are secreted by any glioblastoma cell other than a specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17, secreted by SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines. While any soluble factors secreted by any glioblastoma cells may have some notion of the activity of the "specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification fails to provide any guidance on how to make *any* factors secreted by *any* glioblastoma cell that can be used in a method of specifically inhibiting an immune response to one or more selected antigens.

Moreover, Applicant acknowledge that not all factors secreted by gliomablastoma cells are responsible for the immunosuppression action of GCS (page 15, lines 3-10 and Example 3). Applicant stressed that only specific set of factors disclosed in specification on page 6, lines 5-25 and Table III, page 17 shows immunosuppressive activity when used with APC. In addition, not any glioblastoma cells but only SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines are capable for secreting said factors. For example, Zou et al. (IDS) teach that factors that exert immunologic effects on monocytes and other APC can be produced by some but not all glioblastoma cells (see page 4889 in particular). In addition, Morford et al. (IDS) teach that the exact mechanism by which factors secreted by glioblastoma cells effect APC are unknown and that not every factor, secreted by glioblastoma cells contribute to immunosuppressive effects of glioma culture supernatant (see pages 942 and 943 in particular).

Therefore, there is insufficient direction or objective evidence as to how to make and to how to use *any* factor secreted by *any* glioblastoma cell which will exert immunosuppressive effects on APC for the number of possibilities associated with the myriad of direct and indirect effects associated with immunosuppressive activity of said factors and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to make and use claimed method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to *any* factor secreted by *any* glioblastoma cell correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

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In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

7. Claims 1-17, 25 and 28 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to a specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17, that secreted by SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines.

Applicant is not in possession of : a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to *any* factor secreted by *any* glioblastoma cell.

The specification fails to define *any* factor secreted by *any* glioblastoma cell other than a specific factors disclosed in specification on page 6, lines 5-25 and Table III, page 17, that secreted by SNB19, U251, A 172, A1207, A 1235, A 2781, U 87MG, U138 MG and U373MG cell lines. The lack of sufficient limitations would therefore allow for all other factors secreted by other glioblastoma cells.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of secreted factors may be achieved by means of a recitation of a representative number of secreted factors, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

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Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.) Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1, 3, 4, 6, 13-16 and 28 are rejected under 35 U.S.C. 102(a) as being anticipated by Dix A.R et al (FASEF J, 1999, V13, N.4 pp. A 610).

Dix A.R et al. teach a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to one or more factors secreted by a glioblastoma cells (see Abstract in particular). Dix A.R et al. teach that APC are monocytes obtained from donors blood that can present an autoantigen against which specific inhibition of the immune response is desired (See Abstract in particular).

Claim 6 is included because the claimed functional limitation would be an inherent property of the referenced method of specifically inhibiting an immune response, because the reference method employing the same method steps and same factors secreted by the glioblastoma cells as the claimed methods. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

The reference teaching anticipates the claimed invention.

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10. Claims 1-4, 6, 13-16 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Zou et al. (J of Acquired Immune Deficiency Syndromes and Human Retrovirology, 1997, v.14, page A30).

Zou et al . teach a method of specifically inhibiting an immune response to one or more selected antigens comprising exposing purified or isolated APC to one or more factors secreted by a glioblastoma cells (see Abstract in particular). Zou et al . teach that APC are monocytes obtained from donors blood that can present an autoantigen against which specific inhibition of the immune response is desired (See Abstract in particular).

Claim 6 is included because the claimed functional limitation would be an inherent property of the referenced method of specifically inhibiting an immune response, because the reference method employing the same method steps and same factors secreted by the glioblastoma cells as the claimed methods. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

The reference teaching anticipates the claimed invention.

11. No claim is allowed.

12. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskiy, Ph.D.
Patent Examiner
Technology Center 1600
March 24, 2003

Art Unit: 1644

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

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Michail Belyavskiy, Ph.D.
Patent Examiner
Technology Center 1600
March 24, 2003

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3/24/03